

### REMARKS

Claims 1, 5-27, 31-34 and 37-41 are pending. Claims 13-27, 32-33 and 38-41 are directed to non-elected inventions; their rejoinder is requested upon the allowance of elected claim 1 or 34. The amendments are fully supported by the original disclosure and, thus, no new matter is added by their entry. Elected claims 1 and 34 are amended by incorporating the limitations of claims 2-3 and 35-36, respectively, as well as claim 4 (partial). Claims 6-7 are amended to list separately staphylococcal bacteriophages; new elected claim 37 is based on the present claims 6-7. New non-elected claims 38-41 are based on claims 4 (partial), 13 and 23-24.

#### *Statement of the Substance of the Interview*

The undersigned acknowledges the courtesy extended by the Examiner during the interview on December 14, 2010 (the Interview Summary lists an incorrect date). As stated by the Examiner in her Interview Summary, it was clarified that the present Office Action is not final. The foregoing is Applicants' summary of the interview. If anything else is required to complete the record, do not hesitate to contact the undersigned.

#### *Information Disclosure Statement*

Attached is Form PTO-1449 listing the enclosed documents for the Examiner's consideration. They were first cited in an examination report mailed by the European Patent Office in a counterpart foreign application not more than three months ago. Therefore, the undersigned certifies under 37 CFR § 1.97(e):

"That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement."

This IDS is intended to be in full compliance with the rules, but should the Examiner find any part of its required content to have been omitted, prompt notice to that effect is earnestly solicited, along with additional time under 37 CFR § 1.97(f), to enable Applicants to comply fully. In particular, if any of the listed documents are missing or incomplete, please contact the undersigned who will provide another copy.

As provided by 37 CFR §§ 1.97(g) and (h), the Examiner should not infer that this information and the listed documents are prior art merely because they are submitted for consideration. Further, Applicants do not represent that the claimed subject matter was searched or that this statement encompasses all possible material information.

Consideration of the foregoing and attachments, as well as return of an initialed copy of Form PTO-1449 per M.P.E.P. § 609 to confirm the Examiner's consideration of this information, are earnestly solicited.

### 35 U.S.C. 103 – Nonobviousness

A claimed invention is unpatentable if the differences between it and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art. *In re Kahn*, 78 USPQ2d 1329, 1334 (Fed. Cir. 2006) citing *Graham v. John Deere*, 148 USPQ 459 (1966). The *Graham* analysis needs to be made explicitly. *KSR Int'l v. Teleflex*, 82 USPQ2d 1385, 1396 (2007). It requires findings of fact and a rational basis for combining the prior art disclosures to produce the claimed invention. See *id.* ("Often, it will be necessary for a court to look to interrelated teachings of multiple patents . . . and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue"). The use of hindsight reasoning is impermissible. See *id.* at 1397 ("A factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon *ex post* reasoning"). Thus, a *prima facie* case of obviousness requires "some rationale, articulation, or reasoned basis to explain why the conclusion of obviousness is correct." *Kahn* at 1335; see *KSR* at 1396. An inquiry should be made as to "whether the improvement is more than the predictable use of prior art elements according to their established functions." *Id.* But a claim that is directed to a combination of prior art elements "is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." *Id.* Finally, a determination of *prima facie* obviousness requires a reasonable expectation of success. See *In re Rinehart*, 189 USPQ 143, 148 (C.C.P.A. 1976).

Claims 1-5, 8-12, 31 and 34-36 were rejected under Section 103(a) as allegedly unpatentable over Hogset et al. (WO 02/44395) in view of Embleton et al. (J. Antimicrobiol. Chemotherap. 50:857-864, 2002). Applicants traverse because the subject matter claimed in this application would not have been obvious from the cited disclosures.

First, one of ordinary skill in the art, at the time the claimed invention was made, would not have combined the Hogset and Embleton disclosures as proposed in the Office Action. Second, Applicants' claimed composition has unexpected properties that would not have been predicted from the prior art.

The present claims 1 and 34 are directed to a composition comprising a conjugate of (i) a photosensitizer selected from the group consisting of chlorins and phenothiaziniums and (ii) a staphylococcal bacteriophage, wherein the photosensitizer is covalently linked to the bacteriophage. The Examiner acknowledged that neither Hogset nor Embleton discloses the presently claimed conjugate.

Hogset discloses a method for introducing a molecule into a cell comprising: contacting the cell with a photosensitising agent, contacting the cell with the molecule to be introduced associated with a carrier, and irradiating the cell with light of a wavelength effective to activate the photosensitising agent. The cited document suggests bacteriophages as one example of the carrier for the molecule to be introduced (page 10, lines 24-26). Bacteriophages are also mentioned as one example of an optional carrier for the photosensitising agent (page 20, line 21, to page 21, line 1).

Hogset fails to teach nor would it have made obvious to select a staphylococcal bacteriophage as the carrier. The cited document also does not disclose linking a photosensitizer and a bacteriophage by covalent bonding, still less wherein the photosensitizer is selected from the group consisting of chlorins and phenothiaziniums.

Applicants note that Hogset is concerned with delivery of a molecule into a eukaryotic cell (page 6, lines 22-29) with the aim of internalisation of a molecule of interest into the eukaryotic cell. Thus, the cited document suggests use of a bacteriophage only in the context of use as a viral carrier for delivery to eukaryotic cells. In this context, bacteriophages are not used to target bacteria, which are prokaryotic, nor are bacteriophages used to assist in killing bacteria.

Embleton is concerned with targeting and killing bacteria (i.e., prokaryotic cells). Applicants submit that one of ordinary skill in the art would not have combined Hogset with Embleton to find an improved conjugate capable of targeting and killing bacteria because there was no reasonable expectation that the same methods would succeed for prokaryotes and eukaryotes. As explained in the attached Declaration of Professor Wilson at paragraph 12, even a skilled person would not have considered a document concerned with delivery of a molecule of interest into eukaryotic cells relevant to consideration of targeting and killing prokaryotic cells. Therefore, one of ordinary skill in the art would not have read these documents together or combined them as proposed.

Even if the disclosures of Hogset and Embleton were combined, one of ordinary skill in the art would not have had any reasonable expectation of success to improve targeting and photosensitizer-mediated killing of bacteria as required by Embleton since Hogset only teaches use of bacteriophage as a carrier for delivery to eukaryotic cells. In other words, Hogset does not teach or make obvious the use of bacteriophage to target a photosensitizer to bacteria and then to kill them.

Attached are the Declaration of Professor Wilson ("Wilson Declaration") and a document cited therein, Embleton et al. ("Development of a novel targeting system for lethal photosensitization of antibiotic-resistant strains of *Staphylococcus aureus*" *Anti-microbial Agents and Chemotherapy* 49:3690-3696, 2005). The Examiner's consideration of the attachments is requested because they show that Applicants' claimed composition has properties that would not have been expected from the prior art. Citing KSR, the Manual of Patent Examining Procedure states at Section 2141-I:

When considering obviousness of a combination of known elements, the operative question is thus "whether the improvement is more than the predictable use of prior art elements according to their established functions."

In paragraphs 5 to 10 of the Wilson Declaration, it is explained that covalently linking a staphylococcal bacteriophage to a photosensitizer selected from the group consisting of chlorins and phenothiaziniums provides a composition that is unexpectedly better than Embleton's antibody-photosensitizer conjugate in at least three respects: (1) improved killing of bacteria, (2) killing of bacteria in all three growth phases, and (3) killing in the presence of an antibiotic. Professor Wilson, who is an expert in the field of the claimed

invention, considers that these properties would not have been predictable from the prior art. Thus, even if prima facie obvious, the attached evidence proves the present claims are patentable.

Finally, the dependent claims are patentable over Hogset in view of Embleton because their combined disclosures do not render obvious all limitations of independent claim 1 or 34. In other words, claims 5, 8-12 and 31 are not obvious from the cited documents because the limitations of an independent claim are incorporated in its dependent claims. M.P.E.P. § 2143.03 citing *In re Fine*, 5 USPQ2d 1596 (Fed. Cir. 1988).

Therefore, for the above reasons, one of ordinary skill in the art would not have found Applicants' present claims obvious over Hogset and Embleton.

Claims 1-12, 31 and 34-36 were rejected under Section 103(a) as allegedly unpatentable over Hogset et al. (WO 02/44395) in view of Embleton et al. (J. Antimicrobiol. Chemotherap. 50:857-864, 2002), and further in view of Norris et al. (US 2004/0220123). Applicants traverse because the subject matter claimed in this application would not have been obvious from the cited disclosures.

First, one of ordinary skill in the art, at the time the claimed invention was made, would not have combined the Hogset, Embleton, and Norris disclosures as proposed in the Office Action. Second, as explained above, Applicants' claimed composition has unexpected properties that would not have been predicted from the prior art.

Hogset and Embleton are discussed above. Further, Norris does not teach or make obvious covalently linking a staphylococcal bacteriophage to a toxic agent, still less to a photosensitizer selected from the group consisting of chlorins and phenothiaziniums. In fact, Norris is not concerned with photodynamic therapy at all. Thus, Applicants submit that Norris would not have been combined with Hogset and Embleton, nor would one of ordinary skill in the art have had any reasonable expectation of success to improve photodynamic therapy using the claimed composition.

The attached Wilson Declaration and Embleton et al. ("Development of a novel targeting system for lethal photosensitization of antibiotic-resistant strains of *Staphylococcus aureus*" Antimicrobial Agents and Chemotherapy 49:3690-3696, 2005) proves Applicants' claimed invention is patentable because (1) improved killing of bacteria, (2)

killing of bacteria in all three growth phases, and (3) killing in the presence of an anti-biotic would not have been expected from the prior art.

Finally, the dependent claims are patentable over Hogset in view of Embleton and Norris because their combined disclosures do not render obvious all limitations of independent claim 1 or 34. In other words, claims 5-12 and 31 are not obvious from the cited documents because the limitations of an independent claim are incorporated in its dependent claims. M.P.E.P. § 2143.03 citing *In re Fine*, 5 USPQ2d 1596 (Fed. Cir. 1988).

Therefore, for the above reasons, one of ordinary skill in the art would not have found Applicants' present claims obvious over Hogset, Embleton, and Norris.

Withdrawal of the Section 103 rejections is requested.

#### *Conclusion*

Having fully responded to the pending Office Action, Applicants submit that the claims are in condition for allowance and earnestly solicit an early Notice to that effect. The Examiner is invited to contact the undersigned if additional information is required.

Respectfully submitted,

**NIXON & VANDERHYE P.C.**

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